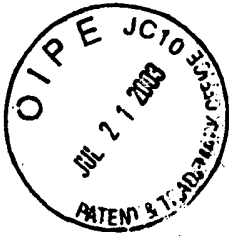


1634



PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of : Mitts et al.  
Serial No. : 09/580,110  
Filing Date : May 30, 2000  
Examiner : Sheinberg, Monika B  
Art Unit : 1634  
Docket No. : 25812-13  
Title : Elastin Peptide Analogs and Uses of Same in Combination with Skin Enhancing Agents

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## EFFECTS OF ADRENERGIC AGONISTS ON ELASTIN AND COLLAGEN PRODUCTION

Figure 9a shows accumulations of elastin and collagen for treated and non-treated smooth muscle cells over the 6 day period: 1) There is a significant and approximately equal accumulation of collagen under both conditions of stimulation representing a 50% increase. 2) Elastin also increases significantly with both alpha and beta adrenergic stimulation but the response is twice greater with the alpha than with beta adrenergic agonists. In figure 9b we show the relationships of these increases to the formation of crosslinks: 3) Beta adrenergic stimulation significantly enhances the crosslink ratios per cell as well as the crosslink ratio per unit of insoluble elastin. 4) Alpha stimulation, on the other hand did not significantly affect the crosslink per cell ratio value but significantly depresses the crosslink:elastin ratio value. 5) We therefore demonstrate a reverse effect between the alpha and beta agonists; in essence, we have uncoupled the formation of elastin and the formation of crosslinks of elastin. 6) This new information is in sharp contrast to that of Mecham et al <sup>19</sup> who studied the effects of cyclic nucleotides on elastin synthesis in ligamentum nuchae fibroblasts and reported that beta adrenergic stimulation did not affect elastin production. Clearly, their cell type differs in behavior from the rat smooth muscle cell system which we are using.

## ACKNOWLEDGEMENTS

This research was supported by grants from the Veterans' Administration and Loma Linda University. We gratefully acknowledge the expert technical assistance of L. Stell and A. MacMurray.

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